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NOTICE OF ALLOWANCE AND FEE(S) DUE

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12/22/2009

VERTEX PHARMACEUTICALS INC. 130 WAVERLY STREET CAMBRIDGE, MA 02139-4242 EXAMINER

ZHOU, SHUBO

ART UNIT PAPER NUMBER

1631

DATE MAILED: 12/22/2009

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/790,507 | 03/01/2004 | Albert Pierce | VPI/03-12 US | 1051 |

TITLE OF INVENTION: TARGET LIGAND GENERATION

| APPLN. TYPE | SMALL ENTITY | ISSUE FEE DUE | PUBLICATION FEE DUE | PREV. PAID ISSUE FEE | TOTAL FEE(S) DUE | DATE DUE |
|----------------|--------------|---------------|---------------------|----------------------|------------------|------------|
| nonprovisional | NO | \$1510 | \$300 | \$0 | \$1810 | 03/22/2010 |

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE

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| appropriate. All further indicated unless correcte maintenance fee notificat | correspondence includin d below or directed oth | g the Patent, advance of the lerwise in Block 1, by (a | rders and notification of a) specifying a new con | f maintena respondenc | nce fees will be address; an | be mailed to the current d/or (b) indicating a sep | correspondence address as arate "FEE ADDRESS" for |
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| VERTEX PHA 130 WAVERLY CAMBRIDGE, I | | | I S a tr | hereby cer tates Postal ddressed to ansmitted t | Certifictify that this I I Service with The Mail Stothe USPTO | cate of Mailing or Trans Fee(s) Transmittal is bein sufficient postage for fir op ISSUE FEE address (571) 273-2885, on the G | smission g deposited with the United st class mail in an envelope above, or being facsimile tate indicated below. |
| | | | | | | | (Depositor's name) |
| | | | | | | | (Signature) |
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| APPLICATION NO. | FILING DATE | | FIRST NAMED INVENT | OR | A' | TTORNEY DOCKET NO. | CONFIRMATION NO. |
| 10/790,507 | 03/01/2004 | • | Albert Pierce | | | VPI/03-12 US | 1051 |
| TITLE OF INVENTION | | | T | T | | | |
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| nonprovisional | NO | \$1510 | \$300 | _ | \$0 | \$1810 | 03/22/2010 |
| EXAM | INER | ART UNIT | CLASS-SUBCLASS | ╝ | | | |
| ZHOU, S | SHUBO | 1631 | 703-011000 | | | | |
| "Fee Address" indi PTO/SB/47; Rev 03-0 Number is required. 3. ASSIGNEE NAME ADDRESSED NOTE: Unl | ess an assignee is identi n in 37 CFR 3.11. Comp | 'Indication form ed. Use of a Customer A TO BE PRINTED ON | data will appear on the | atively, ngle firm (her agent) an ttorneys or be printed. ttype) e patent. If an assignment | naving as a mond the names of agents. If no agents. an assignee ent. | ember a 2 | locument has been filed for |
| 4a. The following fee(s) a Issue Fee Publication Fee (N | | 4l permitted) | b. Payment of Fee(s): (P A check is enclosed Payment by credit | lease first: d. card. Form | reapply any p | previously paid issue fee attached. the required fee(s), any do | , |
| a. Applicant claims | tus (from status indicated s SMALL ENTITY statu d Publication Fee (if reque ecords of the United Sta | is. See 37 CFR 1.27. | ☐ b. Applicant is no l | onger clain | ning SMALL | ENTITY status. See 37 C | |
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| This collection of informan application. Confident submitting the completed his form and/or suggesti | ation is required by 37 C iality is governed by 35 I application form to the ons for reducing this bu | FR 1.311. The informatic U.S.C. 122 and 37 CFR USPTO. Time will vary | on is required to obtain on the control of the cont | or retain a b estimated t dividual ca ficer, U.S. I | penefit by the penefit benefit by the penefit by the penefit benefit by the penefit benefit by the penefit by the penefit benefit by the penefit by the penefit benefit benefit by the penefit benefit benefit by the pene | public which is to file (an utes to complete, including nents on the amount of ti- demark Office, U.S. Der | d by the USPTO to process) ng gathering, preparing, and me you require to complete partment of Commerce, P.O. for Patents, P.O. Box 1450, |

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| 27916 | 7590 | 12/22/2009 | | EXAM | INER |
| VERTEX PHARMACEUTICALS INC. | | | | ZHOU, | SHUBO |
| 130 WAVERLY | | | | ART UNIT | PAPER NUMBER |
| CAMBRIDGE, M | 1A 02139-424 | 4 2 | | 1631 | |
| | | | | DATE MAILED: 12/22/200 | 9 |

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

| | Application No. | Applicant(s) | | |
|--|--|---|--|--|
| | 10/790,507 | PIERCE ET AL. | | |
| Notice of Allowability | Examiner | Art Unit | | |
| | CULIDO (Ioo) 7HOH | 1621 | | |
| | SHUBO (Joe) ZHOU | 1631 | | |
| The MAILING DATE of this communication apperature All claims being allowable, PROSECUTION ON THE MERITS IS herewith (or previously mailed), a Notice of Allowance (PTOL-85) NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RI of the Office or upon petition by the applicant. See 37 CFR 1.313 | (OR REMAINS) CLOSED in this a or other appropriate communicati GHTS. This application is subject | application. If not included on will be mailed in due course. THIS | | |
| 1. \boxtimes This communication is responsive to <u>amendment filed 11/2</u> | <u>20/09</u> . | | | |
| 2. \boxtimes The allowed claim(s) is/are $\underline{1-4,6-12,14-16,19,20,24-39}$ and | <u>d 42-46</u> . | | | |
| 3. Acknowledgment is made of a claim for foreign priority ur a) All b) Some* c) None of the: 1. Certified copies of the priority documents have 2. Certified copies of the priority documents have 3. Copies of the certified copies of the priority documents | been received. been received in Application No. | | | |
| International Bureau (PCT Rule 17.2(a)). | | | | |
| * Certified copies not received: | | | | |
| Applicant has THREE MONTHS FROM THE "MAILING DATE" noted below. Failure to timely comply will result in ABANDONN THIS THREE-MONTH PERIOD IS NOT EXTENDABLE. | | ly complying with the requirements | | |
| 4. A SUBSTITUTE OATH OR DECLARATION must be subm INFORMAL PATENT APPLICATION (PTO-152) which give | | | | |
| 5. CORRECTED DRAWINGS (as "replacement sheets") mus | st be submitted. | | | |
| (a) \square including changes required by the Notice of Draftspers | on's Patent Drawing Review (PT | O-948) attached | | |
| 1) 🔲 hereto or 2) 🔲 to Paper No./Mail Date | | | | |
| (b) ☐ including changes required by the attached Examiner's Paper No./Mail Date | s Amendment / Comment or in the | e Office action of | | |
| Identifying indicia such as the application number (see 37 CFR 1 each sheet. Replacement sheet(s) should be labeled as such in t | | | | |
| 6. DEPOSIT OF and/or INFORMATION about the depo attached Examiner's comment regarding REQUIREMENT | | | | |
| | | | | |
| Attachment(s) | - - | | | |
| 1. Notice of References Cited (PTO-892) | 5. | , , | | |
| 2. Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No./Mail [| Date | | |
| 3. Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date | 7. 🛛 Examiner's Amer | ndment/Comment | | |
| Examiner's Comment Regarding Requirement for Deposit 8. Examiner's Statement of Reasons for Allowance of Biological Material | | | | |
| | 9. Other | | | |
| /SHUBO (Joe) ZHOU/ | | | | |
| Primary Examiner, Art Unit 1631 | | | | |
| | | | | |

Examiner's Statement and Reasons for Allowance

Examiner's Statement and Amendment

The amendment to the claims filed on 11/20/09 is acknowledged and has been entered.

The rejection under 35 USC 112, second paragraph, is withdrawn in view of applicant's amendment filed 11/20/09.

The rejection under 35 USC 101 is withdrawn in view of the examiner's amendment (below) as the claimed process is tied to a particular machine – the suitably programmed computer.

Claims 1-4, 6-12, 14-16, 19-20, 24-39, and 42-46 are allowed with the following examiner's amendment.

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Michael DiVerdi on 12/15/09.

In the claims (based on the amended claims filed 11/20/09):

In claim 1:

In lines 6-7, after "set by" in line 6, delete "an amino acid homologous structural feature of 25% or greater for proteins or", and insert -- 25% or more sequence homology for proteins, or by --;

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In the last line of claim 1, after "(4)", insert -- wherein steps (1) through (5) are performed by a suitably programmed computer --.

In claim 16:

In lines 2-3, delete "homologous feature comprises structural homology between the proteins of at least 40% amino acid homology," and insert therefor -- sequence homology for proteins is at least 40% --.

In claim 19:

In line 1, after "wherein the," delete "homology," and insert therefor -- structural information --.

In claim 32:

In line 2, after "target," delete "macromolecule," and insert therefor -- protein --; In line 3, after "target," delete "macromolecule," and insert therefor -- protein --.

In claim 39:

In line 4, after "comprising", delete "an amino acid homologous structural feature of", and insert after "25% or greater" -- sequence homology --;

In the last line of claim 39, after "(5)", insert -- wherein steps (1) through (6) are performed by a suitably programmed computer --.

In claim 42:

In lines 8-9, after "set by" in line 8, delete "an amino acid homologous structural feature of 25% or greater for proteins or", and insert -- 25% or more sequence homology for proteins, or by --.

In claim 43:

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Art Unit: 1631

In lines 6-7, after "set by" in line 6, delete "an amino acid homologous structural feature of 25% or greater for proteins or", and insert -- 25% or more sequence homology for proteins, or by --.

In the specification (originally filed 3/1/04):

On page 19, line 11, after "Viewer (", delete "http://www.".

Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran, can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Shubo Zhou/

Shubo (Joe) Zhou, Ph.D. Primary Examiner, Art Unit 1631 571-272-0724 Application/Control Number: 10/790,507

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